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Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L4

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DATE: Monday, March 14, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L4	L3 and 424/450.ccls.	9	L4
L3	(nucleic or dna or rna) same (encapsulat$) same (liposome) same (protamine or histone or polyornithine or polylysine or spermine or spermidine)	157	L3
L2	(nucleic or dna or rna) same (encapsulat$) same (liposome) same (protamine or histone or polyornithinge or polylysine or spermine or spermidine)	157	L2
L1	(nucleic or dna or rna) same encapsulat$ same liposome	2608	L1

END OF SEARCH HISTORY

L3: Entry 143 of 157 File: USPT Jun 1, 1999

DOCUMENT-IDENTIFIER: US 5908777 A
TITLE: Lipidic vector for nucleic acid delivery

Detailed Description Text (21):
In accordance with the present invention, the aforementioned 20-mer peptide, with its three negatively charged glutamic acid residues, was added to a positively charged DNA/polylysine complex at a DNA/polylysine/20-mer peptide ratio of 1:0.75:0.4 (wt:wt:wt). The resultant complex then was encapsulated into anionic liposomes composed of DOPE/CHEMS/folate-PEG-PE (6:4:0.01) at a lipid/DNA ratio of 12:1 (wt:wt). These DNA-containing liposomes were highly effective in transfecting receptor-bearing KB cells, and remained effective in the presence of 10% fetal bovine serum. By contrast, liposomes lacking the 20-mer peptide lost transfection effectiveness in the presence of serum.

Detailed Description Text (30):
DNA/polylysine (1:0.75) complex became spontaneously encapsulated when rapidly mixed with DOPE/CHEMS (6:4) liposomes. The size of the DNA-containing liposome was dependent on the charge ratio between the DNA/polylysine complex and the anionic liposomes (FIG. 3). When the overall charge was close to neutral, the size of the particles increased over time due to aggregation. A similar charge/size relationship was observed when 0.1 mole % folate-PEG-PE was included in the anionic liposomes during the preparation of folate-targeted liposomes. In order to compare the liposome preparations described above with standard preparations, a cationic liposome DNA/DC-chol complex was prepared according to Gao and Huang, Biochem. Biophys. Res. Comm. 179: 280-85 (1991). Its activity was deemed optimum when prepared at a ratio of 1 .mu.g:10 nM of DNA to liposome.

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L4: Entry 2 of 9 File: USPT Apr 16, 2002

DOCUMENT-IDENTIFIER: US 6372250 B1
TITLE: Non-invasive gene targeting to the brain

Detailed Description Text (5):
The number of therapeutic genes encapsulated within the liposome may vary from 1 to many, depending on the disease being treated. The limiting factor will be the diameter of therapeutic gene that is encapsulated within the liposome. Using polycationic proteins such as histone, protamine, or polylysine, it is possible to compact the size of plasmid DNA that contains several thousand nucleotides to a structure that has a diameter of 10-30 nm. The volume of a 100 diameter liposome is 1000-fold and 35-fold greater than the volume of a 10 nm and 30 nm DNA compacted sphere, respectively. Therefore, it is possible to encapsulate many copies of the same gene or multiple copies of multiple genes within the liposome.

Current US Original Classification (1):
424/450

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L4: Entry 7 of 9 File: USPT Aug 29, 2000

DOCUMENT-IDENTIFIER: US 6110490 A
TITLE: Liposomal delivery system for biologically active agents

Detailed Description Text (144):
Preparation of the DLS Liposomes. Liposomes were formed by mixing 1 mg dioctadecyl-amidoglycyl spermidine and 1 mg dioleoyl-phosphatidyl ethanolamine. After thorough stirring, the mixture was evaporated to dryness in a round-bottomed borosilicate tube using a rotary vortex evaporator under vacuum. Then the dry lipid film was hydrated with a maximum volume (60 .mu.l/mg lipid) of a solution containing 160 .mu.g plasmid DNA and was slightly vortexed. After incubation at room temperature for 15 min, the resulting suspension was vigorously mixed by vortex. Subsequent liposomal DNA preparation was then diluted in 150 mM NaCl, and kept at 4.degree. C. Liposomes appeared to range from 200 to 3,000 nm in diameter as determined by transmission electronic microscopy. DLS liposomes consist of multilamellar bilayers vesicles which may complex as well as encapsulate DNA. The entrapment rate was found to be 88.+-.8% (mean .+-.S.D.) of the initial DNA input dose. This type of liposomes were used in examples 14-17.

Current US Original Classification (1):
424/450

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L4: Entry 8 of 9 File: USPT Jun 1, 1999

DOCUMENT-IDENTIFIER: US 5908777 A
TITLE: Lipidic vector for nucleic acid delivery

Detailed Description Text (21):
In accordance with the present invention, the aforementioned 20-mer peptide, with its three negatively charged glutamic acid residues, was added to a positively charged DNA/polylysine complex at a DNA/polylysine/20-mer peptide ratio of 1:0.75:0.4 (wt:wt:wt). The resultant complex then was encapsulated into anionic liposomes composed of DOPE/CHEMS/folate-PEG-PE (6:4:0.01) at a lipid/DNA ratio of 12:1 (wt:wt). These DNA-containing liposomes were highly effective in transfecting receptor-bearing KB cells, and remained effective in the presence of 10% fetal bovine serum. By contrast, liposomes lacking the 20-mer peptide lost transfection effectiveness in the presence of serum.

Detailed Description Text (30):
DNA/polylysine (1:0.75) complex became spontaneously encapsulated when rapidly mixed with DOPE/CHEMS (6:4) liposomes. The size of the DNA-containing liposome was dependent on the charge ratio between the DNA/polylysine complex and the anionic liposomes (FIG. 3). When the overall charge was close to neutral, the size of the particles increased over time due to aggregation. A similar charge/size relationship was observed when 0.1 mole % folate-PEG-PE was included in the anionic liposomes during the preparation of folate-targeted liposomes. In order to compare the liposome preparations described above with standard preparations, a cationic liposome DNA/DC-chol complex was prepared according to Gao and Huang, Biochem. Biophys. Res. Comm. 179: 280-85 (1991). Its activity was deemed optimum when prepared at a ratio of 1 .mu.g:10 nM of DNA to liposome.

Current US Cross Reference Classification (2):
424/450

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L4: Entry 9 of 9 File: USPT Jun 1, 1999

DOCUMENT-IDENTIFIER: US 5908635 A
TITLE: Method for the liposomal delivery of nucleic acids

Brief Summary Text (15):
The liposome compositions of the present invention provide highly efficient delivery of nucleic acids to cells. Liposome vesicles are prepared from a mixture of a cationic lipopolyamine and a neutral lipid. Nucleic acids are associated with the liposomes in two ways: (1)complex formation between the cationic liposome vesicle and negatively charged nucleic acid or (2) partial encapsulation and partial complex formation in and with the cationic liposome vesicle. A preferred embodiment of the present invention uses a spermine-5-carboxy-glycinedioctadecylamide (referred to herein as "DOGS") as the cationic lipopolyamine and dioleylphosphatidyl ethanolamine (referred to herein as "DOPE") as the neutral lipid.

Current US Original Classification (1):
424/450

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☐ 1. Document ID: US 6582725 B2

Using default format because multiple data bases are involved.

L4: Entry 1 of 9 File: USPT Jun 24, 2003

US-PAT-NO: 6582725
DOCUMENT-IDENTIFIER: US 6582725 B2

TITLE: Human PEA3 is a tumor suppressor for cancer cells

DATE-ISSUED: June 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Xing; Xiangming	Sugar Land	TX		
Hung; Mien-Chie	Houston	TX		

US-CL-CURRENT: 424/450; 424/93.1, 424/93.2, 424/93.6, 435/320.1, 435/69.1, 514/2, 514/44

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw-De

☐ 2. Document ID: US 6372250 B1

L4: Entry 2 of 9 File: USPT Apr 16, 2002

US-PAT-NO: 6372250
DOCUMENT-IDENTIFIER: US 6372250 B1

TITLE: Non-invasive gene targeting to the brain

DATE-ISSUED: April 16, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pardridge; William M.	Pacific Palisades	CA		

US-CL-CURRENT: 424/450; 435/458, 514/44

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw-De

☐ 3. Document ID: US 6326356 B1

L4: Entry 3 of 9 File: USPT Dec 4, 2001

US-PAT-NO: 6326356
DOCUMENT-IDENTIFIER: US 6326356 B1
**** See image for Certificate of Correction ****

TITLE: Suppression of neu overexpression using a mini-E1A gene

DATE-ISSUED: December 4, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hung; Mein-Chie	Houston	TX		
Chen; Hua	Houston	TX		
Yu; Dihua	Houston	TX		

US-CL-CURRENT: 514/44; 424/450, 424/93.2, 424/93.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 4. Document ID: US 6248351 B1

L4: Entry 4 of 9 File: USPT Jun 19, 2001

US-PAT-NO: 6248351
DOCUMENT-IDENTIFIER: US 6248351 B1

TITLE: Human PEA3 is a tumor suppressor for cancer cells

DATE-ISSUED: June 19, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Xing; Xiangming	Sugar Land	TX		
Hung; Mien-Chie	Houston	TX		

US-CL-CURRENT: 424/450; 424/93.2, 424/93.6, 435/320.1, 435/325, 435/375, 435/455, 435/456, 514/2, 514/44, 536/23.1, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 5. Document ID: US 6197754 B1

L4: Entry 5 of 9 File: USPT Mar 6, 2001

US-PAT-NO: 6197754
DOCUMENT-IDENTIFIER: US 6197754 B1
**** See image for Certificate of Correction ****

TITLE: Suppression of tumor growth by a mini-E1A gene

DATE-ISSUED: March 6, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hung; Mien-Chie	Houston	TX		
Chen; Hua	Houston	TX		
Yu; Di-hua	Houston	TX		

US-CL-CURRENT: 514/44; 424/450, 424/93.2, 424/93.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 6. Document ID: US 6172212 B1

L4: Entry 6 of 9 File: USPT Jan 9, 2001

US-PAT-NO: 6172212
DOCUMENT-IDENTIFIER: US 6172212 B1
**** See image for Certificate of Correction ****

TITLE: Pea3 is a tumor suppressor

DATE-ISSUED: January 9, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hung; Mien-Chie	Houston	TX		
Xing; Xiangming	Houston	TX		

US-CL-CURRENT: 536/23.5; 424/450, 424/93.1, 424/93.2, 435/235.1, 435/320.1, 436/71, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐ 7. Document ID: US 6110490 A

L4: Entry 7 of 9 File: USPT Aug 29, 2000

US-PAT-NO: 6110490
DOCUMENT-IDENTIFIER: US 6110490 A

TITLE: Liposomal delivery system for biologically active agents

DATE-ISSUED: August 29, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thierry; Alain R.	Strasbourg			FR

US-CL-CURRENT: 424/450; 424/400

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 8. Document ID: US 5908777 A

L4: Entry 8 of 9 File: USPT Jun 1, 1999

US-PAT-NO: 5908777
DOCUMENT-IDENTIFIER: US 5908777 A

TITLE: Lipidic vector for nucleic acid delivery

DATE-ISSUED: June 1, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lee; Robert J.	Pittsburgh	PA		
Huang; Leaf	Wexford	PA		

US-CL-CURRENT: 435/320.1; 264/4.1, 424/450, 424/93.21, 435/325, 435/458, 435/69.1, 514/44

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 9. Document ID: US 5908635 A

L4: Entry 9 of 9 File: USPT Jun 1, 1999

US-PAT-NO: 5908635
DOCUMENT-IDENTIFIER: US 5908635 A

TITLE: Method for the liposomal delivery of nucleic acids

DATE-ISSUED: June 1, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thierry; Alain	Bethesda	MD		

US-CL-CURRENT: 424/450; 424/400

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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Terms	Documents
L3 and (424/450).ccls.	9

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L3: Entry 155 of 157 File: USPT Feb 16, 1993

DOCUMENT-IDENTIFIER: US 5187260 A
TITLE: Process for the preparation of a high purity protamine-DNA complex and process for use of same

Abstract Text (1):
A process is disclosed in which high purity protamine-DNA complexes are prepared by collecting nucleoprotamines specific developmental stages of a life form, specifically, amphibian, egg by low temperature processing. The process also includes the steps of sequential homogenization in a high concentration aqueous salt solution at a buffered low pH, followed by ultracentrifugation to remove insoluble matter. Either a crude mixture or pure isolate of the complexes may be produced. Pure isolates require aqueous chloroform extraction to isolate protein and to remove lipids. Lyophilization then removes chloroform and excess water. The isolate is then fractionated by single pass alumina chromatography. Dialysis against pure water removes salts. Repeated lyophilization removes excess water and concentrates single protamines and protamine-like proteins. The mixture may then be reconstituted with 5% weight/volume heterologous or homologous DNA, in order to shield from charge toxicity. Crude mixtures may be produced by precipitating the supernate of ultracentrifugation in pure water, followed by ultracentrifugation to sediment in solids. Lyophilization then removes any water from the damp solids. The crude solids are suitable for oral use, especially if utilized in gelatin capsules. Sterile filtration to injection quality aqueous form. Following isolation of the protamine-DNA complex, encapsulation of the prepared solid or aqueous protamine-DNA complexes in a specific carrier substance may be accomplished, depending upon the target tissue for the protamine. Several encapsulation carriers are known from prior art literature, such as, for example, liposomes and nanoparticles. The protamine-DNA complexes of the present invention are useful in inhibiting tumor growth, among other uses.

Brief Summary Text (33):
Following isolation of the protamine-DNA complex, encapsulation of the prepared solid or aqueous protamine-DNA complexes, in a specific carrier substance, may be accomplished, depending upon the target tissue for the protamine. Several encapsulation carriers are known from prior art literature, such as, for example, liposomes and nanoparticles.

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L3: Entry 156 of 157 File: EPAB Aug 19, 1999

DOCUMENT-IDENTIFIER: DE 19859526 A1
TITLE: Pharmaceutical composition, especially for gene transfer and therapy

Abstract Text (1):
CHG DATE=19991202 STATUS=O>A pharmaceutical composition comprising genetic material optionally encapsulated in liposomes as well as starch particles and/or gelatine and/or polymer particles and a contrast agent is new. A pharmaceutical composition comprises: (a) genetic material(s) optionally encapsulated in PEG, immuno, immuno/PEG, cationic or optionally polymer-modified liposomes; (b) lyophilized or degradable starch particles and/or gelatine and/or polymer particles, e.g. nanoparticles; and (c) a contrast agent containing iodine, gadolinium, magnetite or fluorine. The composition can also conveniently contain DNA density-packing proteins, e.g. Nuclear Capsid Protein (NCP 7), HMG and/or synthetic substances, e.g. polyethyleneimine, poly-L-lysine or protamine sulphate. An Independent claims is also included for the preparation of the composition.

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Terms	Documents
L5 and (424/450).ccls.	52

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L6

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Search History

DATE: Monday, March 14, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L6	L5 and 424/450.ccls.	52	L6
L5	(nucleic or dna or rna) same (condens$ or compact$) same (protamine or histone or polyornithine or polylysine or spermine or spermidine)	381	L5
L4	L3 and 424/450.ccls.	9	L4
L3	(nucleic or dna or rna) same (encapsulat$) same (liposome) same (protamine or histone or polyornithine or polylysine or spermine or spermidine)	157	L3
L2	(nucleic or dna or rna) same (encapsulat$) same (liposome) same (protamine or histone or polyornithinge or polylysine or spermine or spermidine)	157	L2
L1	(nucleic or dna or rna) same encapsulat$ same liposome	2608	L1

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L6: Entry 3 of 52 File: USPT Oct 26, 2004

DOCUMENT-IDENTIFIER: US 6808720 B2
TITLE: Charged lipids and uses for the same

Current US Original Classification (1):
424/450

Other Reference Publication (1):
Lee, R.J., et al., "Folate-targeted, anionic liposome-entrapped polylysine-condensed DNA for tumor cell-specific gene transfer," J. Biol. Chem., Apr. 5, 1996, 271(14), 8481-8487.

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L6: Entry 32 of 52 File: USPT Jun 26, 2001

DOCUMENT-IDENTIFIER: US 6251433 B1
TITLE: Polycationic polymers

Brief Summary Text (7):
Condensation facilitates entry of nucleic acids into cell vesicle systems by simulating a macromolecular structure. For example, polylysine condenses DNA into a toroid or doughnut-like structure. (Wagner et al., 1991, Proc. Natl. Acad. Sci. 88:4255-4259).

Detailed Description Text (168):
Examples of polynucleotide binding molecules include: polylysine, polyarginine, polyornithine, and protamine. Examples of organic polycations include: spermine, spermidine, and purtrescine. Other examples include histones, protamines, human serum albumin, DNA binding proteins, non-histone chromosomal proteins, coat proteins from DNA viruses, such as .phi.X174, transcriptional factors also contain domains that bind DNA and therefore may be useful as nucleic aid condensing agents. Briefly, transcriptional factors such as C/CEBP, c-jun, c-fos, AP-1, AP-2, AP-3, CPF, Prot-1, Sp-1, Oct-1, Oct-2, CREP, and TFIID contain basic domains that bind DNA sequences.

Detailed Description Text (220):
The following are examples of useful polypeptides as polycationic agents: polylysine, polyarginine, polyornithine, and protamine. Other examples include histones, protamines, human serum albumin, DNA binding proteins, non-histone chromosomal proteins, coat proteins from DNA viruses, such as .phi.X174, transcriptional factors also contain domains that bind DNA and therefore may be useful as nucleic aid condensing agents. Briefly, transcriptional factors such as C/CEBP, c-jun, c-fos, AP-1, AP-2, AP-3, CPF, Prot-1, Sp-1, Oct-1, Oct-2, CREP, and TFIID contain basic domains that bind DNA sequences.

Current US Cross Reference Classification (1):
424/450

L6: Entry 37 of 52 File: USPT Oct 17, 2000

US-PAT-NO: 6133026
DOCUMENT-IDENTIFIER: US 6133026 A

TITLE: Condensed plasmid-liposome complex for transfection

DATE-ISSUED: October 17, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Huang; Shi Kun	Castro Valley	CA		
Oto; Edwin Kiyoshi	Redwood City	CA		
Hassanipour; Mohammad	Vallejo	CA		
Jin; Bei	Union City	CA		

US-CL-CURRENT: 435/320.1; 424/417, 424/420, 424/450, 435/458, 435/69.1, 536/23.1

CLAIMS:

It is claimed:

1. A composition of plasmid-liposome complexes for use in transfecting a host cell with a gene contained in a plasmid, comprising

condensed plasmid molecules, said molecules condensed with a polycationic condensing agent and suspended in a low-ionic strength aqueous medium, and

cationic liposomes comprising a cationic vesicle-forming lipid,

wherein said complexes have a ratio of liposome lipid to plasmid of greater than 5 nmole liposome lipid/.mu.g plasmid and less than 25 nmole liposome lipid/.mu.g plasmid and have a substantially homogeneous size of less than about 200 nm.

2. The composition of claim 1, wherein the condensed plasmid molecules are DNA plasmid molecules containing a gene selected from the group consisting of genes encoding for cystic fibrosis transmembrane conductance regulator, Factor VIII, interleukin-2 and p53.

3. The composition of claim 1, wherein the condensing agent is a polycation selected from the group consisting of histones, poly-l-glutamine, protamine, melittin and polymyxin B.

4. The composition of claim 3, wherein the condensing agent is a histone selected from total histone, histone 1 and histone 4.

5. The composition of claim 1, wherein the ratio of liposome lipid to plasmid

is between 8-18 nmole liposome lipid/.mu.g plasmid.

6. The composition of claim 1, wherein the low-ionic strength aqueous medium is prepared from a non-ionic osmotic solute.

7. The composition of claim 6, wherein said solute is selected from the group consisting of glucose, sucrose and dextran.

8. The composition of claim 1, wherein the cationic liposomes are composed of a cationic vesicle-forming lipid selected from the group consisting of dimethyldioctadecylammonium (DDAB), 1,2-diolelyloxy-3-(trimethylamino) propane (DOTAP), N-[1-(2,3 ,-ditetradecyloxy)propyl]-N,N-dimethyl-N-hydroxyethylammonium bromide (DMRIE), N-[1-(2,3,-dioleyloxy)propyl]-N,N-dimethyl-N-hydroxy ethylammonium bromide (DORIE), N-[1-(2,3-dioleyloxy) propyl]-N,N,N-trimethylammonium chloride (DOTMA), and 3.beta.[N-(N',N'-dimethylaminoethane) carbamoly] cholesterol (DC-Chol).

9. The composition of claim 1, wherein the cationic liposomes further include a neutral vesicle forming lipid.

10. The composition of claim 1, wherein the cationic liposomes further include cholesterol.

11. The composition of claim 1, wherein the cationic liposomes have a surface coating of hydrophilic polymer chains formed by derivatizing a vesicle-forming lipid, a hydrophilic polymer.

12. The composition of claim 11, wherein at least a portion of the hydrophilic polymer is joined to the vesicle-forming lipid by a bond effective to release the hydrophilic polymer chains in response to an existing or an induced physiologic condition.

13. The composition of claim 11, wherein the plasmid-liposome complexes further include a ligand attached to distal ends of the hydrophilic polymer chains for ligand-specific binding to a receptor molecule on a target cell surface.

14. The composition of claim 11, wherein the hydrophilic polymer is polyethyleneglycol.

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L6: Entry 38 of 52 File: USPT Oct 3, 2000

DOCUMENT-IDENTIFIER: US 6126964 A
TITLE: Process of making a compound by forming a polymer from a template drug

Brief Summary Text (7):
A significant number of multivalent cations with widely different molecular structures have been shown to induce the condensation of DNA. These include spermidine, spermine, Co(NH.sub.3)63+, protamine, histone Hi, and polylysine. (Gosule, L. C. & Schellman, J. A. (1976) Nature 259, 333-335; Chattoraj, D. K., Gosule, L. C. & Schellman, J. A. (1978) J. Mol. Biol. 121, 327-337; Had, N. V., Downing, K. H. & Balhorn, R. (1993) Biochem. Biophys. Res. Commun. 193, 1347-1354; Hsiang, M. W & Cole, R. D. (1977) Proc. Natl. Acad. Sci. USA 74, 4852-4856; Haynes, M., Garret, R. A. & Gratzer, W. B. (1970) Biochemistry 9, 4410-4416; Widom, J. & Baldwin, R. L. (1980) J. Mol. Biol. 144, 431-453.). Quantitative analysis has shown DNA condensation to be favored when 90% or more of the charges along the sugar-phosphate backbone are neutralized (Wilson, R. W. & Bloomfield, V. A. (1979) Biochemistry 18, 2192-2196). Depending upon the concentration of the DNA condensation leads to three main types of structures:

Brief Summary Text (12):
The mechanism of DNA condensation is not obvious. The electrostatic forces between unperturbed helices arise primarily from a counterion fluctuation mechanism requiring multivalent cations and plays the major role in DNA condensation. (Riemer, S. C. & Bloomfield, V. A. (1978) Biopolymers 17, 789-794; Marquet, R. & Houssier, C. (1991) J. Biomol. Struct. Dynam. 9, 159-167; Nilsson, L. G., Guldbrand, L. & Nordenskjold L. (1991) Mol. Phys. 72, 177-192). The hydration forces predominate over electrostatic forces when the DNA helices approach closer then a few water diameters (Leikin, S., Parsegian, V. A., Rau, D. C. & Rand, R. P. (1993) Ann. Rev. Phys. Chem. 44, 369-395). In case of DNA-polymeric polycation interactions, DNA condensation is a more complicated process than the case of low molecular weight polycations. Different polycationic proteins can generate toroid and rod formation with different size DNA at a ratio of positive to negative charge of 0.4 (Garciaramirez, M., & Subirana, J. A. (1994) Biopolymers 34, 285-292). It was shown by fluorescence microscopy that T4 DNA complexed with polyarginine or histone can forms two types of structures; an elongated structure with a long axis length of about 350 nm (like free DNA) and dense spherical particles. (Minagawa, K., Matsuzawa, Y., Yshikawa, K., Matsumoto, M., & Doi, M. (1991) FEBS Lett. 295, 60-67). Both forms exist simultaneously in the same solution. The reason for the co-existence of the two forms can be explained as an uneven distribution of the polycation chains among the DNA molecules. The uneven distribution generates two thermodynamically favorable conformations. (Kabanov, A. V., & Kabanov, V. A. (1995) Bioconjugate Chem. 6, 7-20).

Detailed Description Text (56):
A method of condensing nucleic acid is defined as decreasing the linear length of the nucleic acid. Condensing nucleic acid also means compacting nucleic acid. Condensing nucleic acid also means decreasing the volume which the nucleic acid molecule occupies. A example of condensing nucleic acid is the condensation of DNA that occurs in cells. The DNA from a human cell is approximately one meter in length but is condensed to fit in a cell nucleus that has a diameter of approximately 10 microns. The cells condense (or compacts) DNA by a series of

packaging mechanisms involving the histones and other chromosomal proteins to form nucleosomes and chromatin. The DNA within these structures are rendered partially resistant to nuclease (DNase) action. The condensed structures can also be seen on electron microscopy.

Current US Original Classification (1):
424/450

Other Reference Publication (16):
Hsiang, Myrtle W., et al., "Structure of histone H1-DNA complex: Effect of histone H1 on DNA condensation." Biochemistry 1977; 74; No. 11; 4852-4856.

Other Reference Publication (28):
Sikorav, J.-L., et al., "A Liquid Crystalline Phase in Spermidine-Condensed DNA." Biophysical Journal 1994; 67; 1387-1392.

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L6: Entry 39 of 52 File: USPT Sep 19, 2000

DOCUMENT-IDENTIFIER: US 6120798 A
TITLE: Liposome-entrapped polynucleotide composition and method

Detailed Description Text (14):
It will be appreciated that in embodiments where the polynucleotide is, for example, DNA, the polynucleotide can be condensed using a polycationic condensing agent in addition to or instead of the cationic lipid. For example, spermine, spermidine, histones, poly-lysine and protamine sulfate are polycationic agents suitable for condensing a large polynucleotide to facilitate its entrapment in the liposomes of the invention.

Current US Original Classification (1):
424/450

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L6: Entry 43 of 52 File: USPT May 2, 2000

DOCUMENT-IDENTIFIER: US 6056973 A
TITLE: Therapeutic liposome composition and method of preparation

Detailed Description Text (54):
Polynucleotides, oligonucleotides, other nucleic acids, such as a DNA plasmid, can be entrapped in the liposome by condensing the nucleic acid in single-molecule form. The nucleic acid is suspended in an aqueous medium containing protamine sulfate, spermine, spermidine, histone, lysine, mixtures thereof, or other suitable polycationic condensing agent, under conditions effective to condense the nucleic acid into small particles. The solution of condensed nucleic acid molecules is used to rehydrate a dried lipid film to form liposomes with the condensed nucleic acid in entrapped form. A similar approach to condensing nucleic acids for entrapment in liposomes is described in co-pending U.S. patent application Ser. No. 09/103,341.

Current US Original Classification (1):
424/450

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L6: Entry 52 of 52 File: USPT Apr 6, 1999

DOCUMENT-IDENTIFIER: US 5891468 A
TITLE: Fusogenic liposome compositions and method

Detailed Description Text (122):
Polynucleotides, oligonucleotides, other nucleic acids, such as a DNA plasmid, can be entrapped in the liposome by condensing the nucleic acid in single-molecule form. The nucleic acid is suspended in an aqueous medium containing spermine, spermidine, histone, lysine, mixtures thereof, or other suitable polycationic condensing agent, under conditions effective to condense the nucleic acid into small particles, as described in Example 11. The solution of condensed nucleic acid molecules is used to rehydrate a dried lipid film to form liposomes with the condensed nucleic acid in entrapped form.

Detailed Description Text (211):
DNA plasmid pGL3 (Promega Corporation, Madison, Wis.) is condensed with spermidine (free base, Sigma Chemical Co (St Louis, Mo.)) and then entrapped in fusogenic liposomes as follows.

Current US Original Classification (1):
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